



Gender-related differences in patients with acute heart failure: Management and predictors of in-hospital mortality

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ABSTRACT

Aim and methods: Gender-related differences in clinical phenotype, in-hospital management and prognosis of acute heart failure (AHF) patients have been previously reported in European and US registries. The ALARM-HF survey is the first to include a cohort of 4953 patients hospitalized for AHF in 666 hospitals in 6 European countries, Mexico and Australia.

Results: Women accounted for 37% of the study population, were older and had higher rates of de novo heart failure (45% vs 36%, $p < 0.001$) than men. An acute coronary syndrome (ACS) was the predominant precipitating factor in both genders, but to a lesser extent in females (30% vs 42%, $p < 0.001$). Between genders comparison showed higher incidence of atrial fibrillation, valvular heart disease, diabetes, obesity, anemia and depression in women ($p < 0.05$). Similarly, women had higher left ventricular ejection fraction (LVEF) on admission ($42 \pm 15\%$ vs $36 \pm 13\%$, $p < 0.001$) and systolic blood pressure (135 ± 40 mm Hg vs 131 ± 39 mm Hg, $p = 0.001$) than men. On the other hand, men had more often coronary artery disease, renal failure and chronic obstructive pulmonary disease ($p < 0.05$). Importantly, in-hospital mortality was similar in both genders (11.1% in females vs 10.5% in males, $p = 0.475$), and its common predictors were: systolic blood pressure at admission, creatinine > 1.5 mg/dL and diabetes. Furthermore, recent ACS, valvular heart disease and dementia contributed to prognosis in women, while LVEF, hypertension and anemia were independent predictors in men.

Conclusion: Among patients with AHF, there are significant differences in co-morbidities, precipitating factors and predictors of in-hospital mortality between genders. Nevertheless, in-hospital mortality remains similar between genders.

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1. Introduction

Female patients with cardiovascular disease show distinct characteristics and outcomes and are usually under-treated despite the similar or even better prognosis as compared to men [1,2]. Acute heart failure (AHF) presenting as either decompensated chronic heart failure (HF) or new onset de novo HF is related to poor short- and long-term prognosis [3,4]. AHF shows increasing incidence, however it is not adequately addressed with clinical trials, and so current knowledge mainly derives from large scale registries and surveys. Although numerous prospective clinical trials have investigated various

aspects of chronic HF, women are under-represented in them [5,6]. The EuroHeart Failure Survey II (EHFS II), included patients from 30 European countries and identified gender differences in baseline characteristics, precipitating factors and co-morbidities in patients admitted with AHF [7]. Nevertheless one-year mortality was similar in both genders. Besides this, the Acute Decompensated Heart Failure National Registry (ADHERE) in the United States included patients admitted for AHF in 274 hospitals across the country [8]. ADHERE showed also differences in baseline characteristics and precipitating factors between males and females, however the length of the hospital stay and the in-hospital mortality were similar. Since then, the AHF management has been improved following advances in medical therapies and interventional procedures, while the European Society of Cardiology (ESC) published specific guidelines for the diagnosis and treatment of AHF [9].

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The international Acute Heart Failure Global Registry of Standard Treatment (ALARM-HF) recruited patients from 6 European countries, Australia and Mexico and aimed to describe the characteristics and management of patients hospitalized for AHF [10,11]. The present study constitutes a sub-analysis of ALARM-HF, aiming to explore gender-related differences in clinical characteristics, precipitating factors, co-morbidities, treatment and in-hospital prognosis of patients admitted with AHF in a mixed patient population.

2. Methods

2.1. Study design

The ALARM-HF is a retrospective in-hospital chart audit survey, including patients hospitalized for AHF syndromes in Europe, Latin America and Australia [10,11]. A total of 4953 patients admitted to cardiology departments (67%) or intensive care units (33%) for AHF in 666 hospitals among 9 countries (France 588, Germany 617, Italy 679, Spain 700, UK 623, Greece 255, Turkey 628, Mexico 601 and Australia 262) were enrolled. The participating hospitals were a representative sample according to the geographic region, hospital magnitude (by number of beds), sector (public versus private) and type (academic versus non-teaching status). The study was conducted between October 2006 and March 2007 and the patient's case report forms was completed at or close to discharge every 5–8 consecutive patients. AHF diagnosis was confirmed at discharge according to the definition and classification of ESC guidelines [9].

2.2. Patients' data

Demographic characteristics, past medical history, initial clinical evaluation, diagnostic procedures, medical and interventional treatments, and in-hospital outcomes were obtained. The protocol was approved by the institutional review board of each participating center; however, written informed consent of patients was not required for registry entry, but all data were anonymized.

2.3. Statistical analysis

Data are presented as counts and percent of non-missing values for categorical variables or means and standard deviations (SD) for quantitative variables. Between groups comparison took place using chi-square tests for categorical variables and student's *t*-test or ANOVA Wilcoxon rank-sum tests for quantitative variables. Multivariate logistic regression analysis was used to identify independent prognostic predictors for in-hospital mortality for each gender, separately. Demographics, clinical and laboratory findings at presentation, past medical history, cardiovascular risk factors and medications were forced into the regression model. The odds ratios (OR) and corresponding 95% confidence intervals (CI) are reported for each covariate. All tests were two-sided and results with a *p* value of <0.05 were considered statistically significant. For statistical analysis we used SPSS v13.0 (SPSS Inc., Chicago, Illinois, USA).

3. Results

3.1. Epidemiologic characteristics

Table 1 presents the demographic and clinical characteristics of a total of 4953 patients of both genders (37% females). In the whole cohort, 63.8% had known chronic heart failure, while the rest had de novo AHF. Compared to men, women appeared with AHF at an older age, with higher rates of de novo heart failure ($p < 0.001$). Based on AHF classification, women had less than half the odds to present with cardiogenic shock ($p < 0.001$) and twice the odds to present with right heart failure, as compared to men ($p < 0.001$).

Regarding co-morbidities, women frequently had more atrial fibrillation ($p < 0.001$), valvular heart disease ($p < 0.001$), diabetes mellitus ($p = 0.043$), obesity ($p < 0.001$), anemia ($p < 0.001$) and depression ($p < 0.001$). On the other hand, we observed a lower rate of cardiomyopathy, coronary artery disease (CAD), dyslipidemia, smoking and asthma or chronic obstructive pulmonary disease (COPD) co-existence in women than in men ($p < 0.001$). Arterial hypertension and peripheral vascular disease showed similar rates in both genders (Table 1).

3.2. Precipitating factors

In both genders, acute coronary syndrome (ACS) was the most common precipitating factor. However, women were less likely than

Table 1

Differences in demographic and clinical characteristics, co-morbidities and precipitating factors of acute heart failure between male and female patients.

	Female (n = 1825)	Male (n = 3128)	p value
Age			<0.001
≤50 years	8%	10%	
50–69 years	37%	51%	
>70 years	55%	39%	
Heart failure presentation			<0.001
Acutely decompensated HF	55%	64%	
De novo AHF	45%	36%	
AHF classification			<0.001
Acutely decompensated HF	34%	41%	
Cardiogenic shock	6%	13%	
High cardiac output	1.0%	0.8%	
Hypertensive AHF	13%	5%	
Pulmonary edema	38%	37%	
Right HF	8%	3%	
NYHA class (pre-hospitalization)			0.015
NYHA I	1%	2%	
NYHA II	10%	9%	
NYHA III	36%	35%	
NYHA IV	33%	37%	
Co-morbidities			
Atrial fibrillation/flutter	49%	42%	<0.001
Cardiomyopathy	11%	14%	0.001
Peripheral vascular disease	8%	9%	0.248
CAD	24%	35%	<0.001
Congestive HF	37%	36%	0.451
Valvular heart disease	19%	11%	<0.001
Obesity	30%	25%	<0.001
Diabetes mellitus	47%	44%	0.043
Dyslipidemia	37%	45%	<0.001
Arterial hypertension	70%	70%	0.761
Anemia	17%	13%	<0.001
Depression	11%	7%	<0.001
Renal dysfunction	28%	30%	0.075
Liver disease	3%	4%	0.393
Benign tumor	1%	<1%	0.224
Cancer	3%	3%	0.622
Dementia	6%	3%	<0.001
Asthma/COPD	21%	27%	<0.001
None	41%	44%	0.056
Precipitating factors			
ACS	30%	42%	<0.001
Arrhythmia	29%	26%	0.072
Non compliance	14%	13%	0.260
Infection	18%	15%	0.031
Post surgery	4%	4%	0.240
Valvular heart disease	17%	11%	0.078
Other	15%	13%	<0.001
Other factors			
Smoking	11%	31%	<0.001

HF, heart failure; AHF, acute heart failure; NYHA, New York Heart Association; CAD, coronary artery disease; COPD, chronic pulmonary obstructive disease; ACS, acute coronary syndrome.

men to have ACS ($p < 0.001$) and more likely to have infection ($p = 0.031$) or worsening of valvular heart disease ($p < 0.001$). Arrhythmia onset did not differ between genders ($p = 0.072$).

3.3. Clinical, hemodynamic and laboratory findings (Table 2)

Women appeared on admission with better functional class ($p = 0.015$), higher systolic blood pressure ($p = 0.001$), heart rate ($p = 0.004$) and body mass index ($p = 0.048$). Higher ejection fraction ($p < 0.001$) was found in women's group, while the majority of them

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